# Ebola Outbreak

**Journal Club & MSc Seminar**


Qazvin University of Medical Science
Department of Immunology & Microbiology

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SUPERVISED BY | Dr.M. Aslanimehr


# What you need to know about the deadly outbreak

# BACKGROUND

- Ebola virus disease (**EVD**), formerly known as **Ebola haemorrhagic fever**, is a severe, often fatal illness in humans.
- A 27-year-old Belgian microbiologist named **Peter Piot** and his colleagues were the first to scientifically identify the Ebola virus.
- Ebola virus disease (EVD) first appeared in **1976** in **2 simultaneous outbreaks**, one in **Nzara**, **Sudan**, and the other in **Yambuku**, **Democratic Republic of Congo**. The latter occurred in **a village near the Ebola River**, from which the disease takes its name.
- The **current outbreak** in west Africa, (**first cases notified in March 2014**), is **the largest and most complex Ebola outbreak** since the Ebola virus was first discovered in 1976. There have been more cases and deaths in this outbreak than all others combined.
- It has also spread between countries starting in **Guinea** then spreading across land borders to **Sierra Leone** and **Liberia**, by air (1 traveller only) to **Nigeria**, and by land (1 traveller) to **Senegal**.
- The **average** EVD case fatality rate is around **50%**. Case fatality rates have varied from **25% to 90%** in **past outbreaks.**

1976

Ebola first appeared in 1976 in 2 simultaneous outbreaks, in Nzara, Sudan...

**The Ebola River** Go to Article


...and in Yambuku, Democratic Republic of Congo. The latter was in a village situated near the Ebola River, from which the disease takes its name.



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## Case Counts*

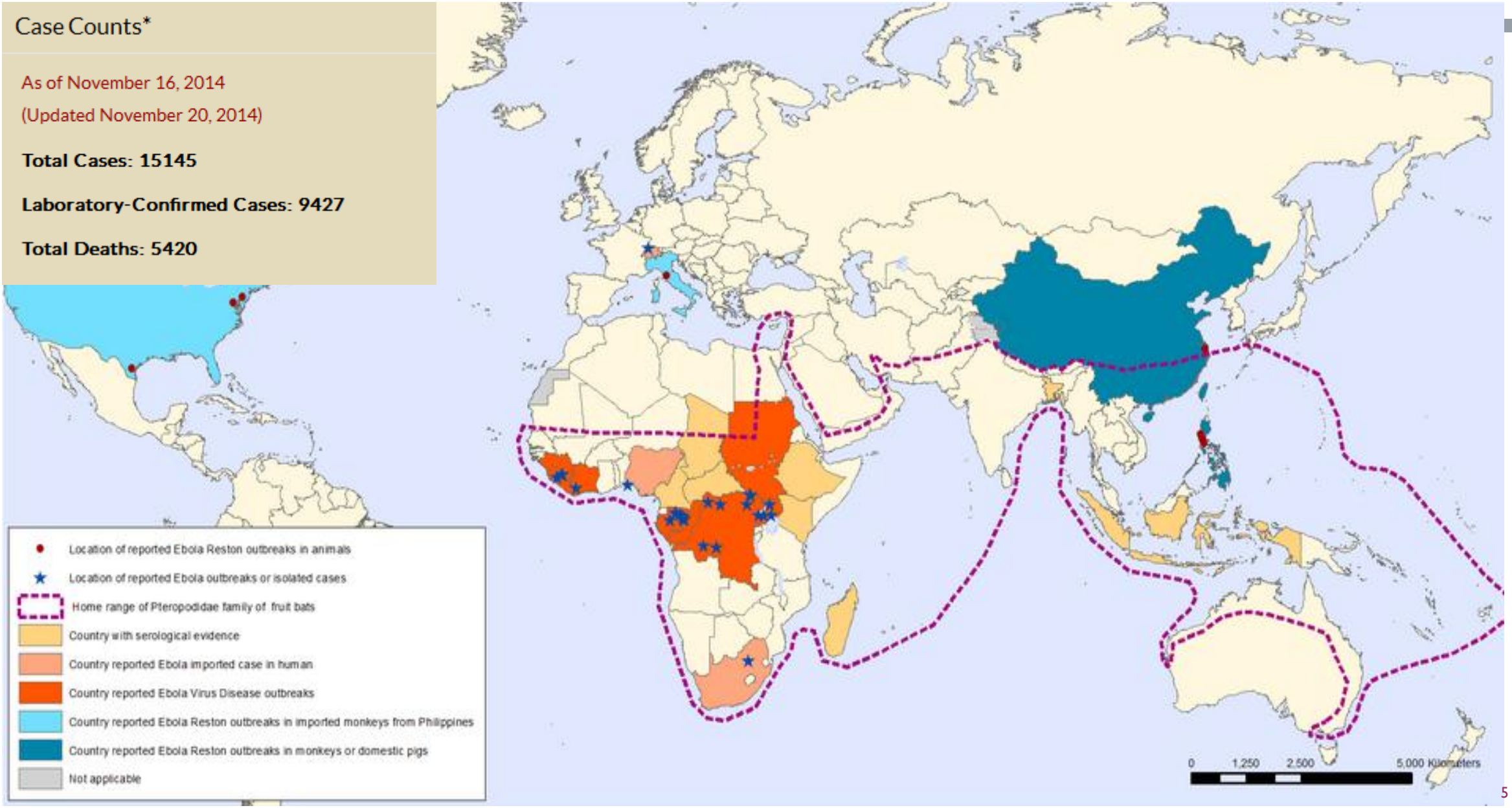
As of November 16, 2014

(Updated November 20, 2014)

**Total Cases: 15145**

**Laboratory-Confirmed Cases: 9427**

**Total Deaths: 5420**



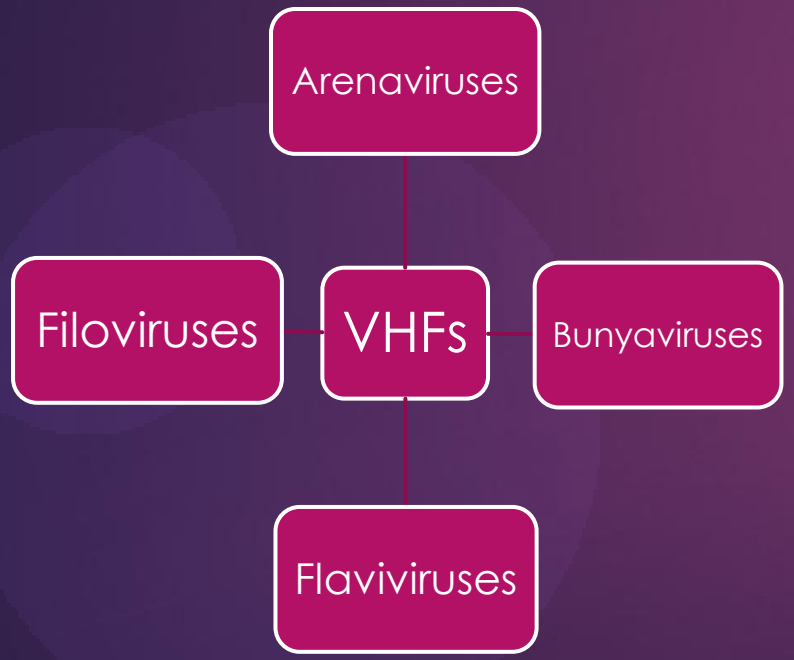
# What are viral hemorrhagic fevers?

- Viral hemorrh… …es that are caused by several dis… …**"viral hemorrhagic** …em syndrome. Characteristic… …ed, and the body's ability to regu… …often accompanie…
- The Special P… …hemorrhagic fever viruses that ar… …athogens The Division of Ve… …lational Center for Infectious Dise… …cause two other hemorrhagic … …**low fever**.

**Diseases handled by VSPB**

- Alkhurma homorrhagic fever (AHF)
- Chapare hemorrhagic fever (CHHF)
- Crimean-Congo hemorrhagic fever (CCHF)
- Ebola hemorrhagic fever
- Hemorrhagic fever with renal syndrome (HFRS)
- Hantavirus pulmonary syndrome (HPS)
- Hendra virus disease
- Kyasanur Forest disease (KFD)
- Lassa fever
- Lujo hemorrhagic fever (LUHF)
- Lymphocytic choriomeningitis (LCM)
- Marburg hemorrhagic fever
- Nipah virus encephalitis
- Omsk hemorrhagic fever (OHF)
- Rift Valley fever (RVF)
- Tick-borne encephalitis

VHFs are caused by viruses of **four** distinct families




1. They are all RNA viruses, and all are covered, or enveloped, in a fatty (lipid) coating.
2. Their survival is dependent on an animal or insect host, called the natural reservoir.
3. The viruses are geographically restricted to the areas where their host species live.
4. Humans are not the natural reservoir for any of these viruses. Humans are infected when they come into contact with infected hosts. However, with some viruses, after the accidental transmission from the host, humans can transmit the virus to one another.
5. Human cases or outbreaks of hemorrhagic fevers caused by these viruses occur sporadically and irregularly. The occurrence of outbreaks cannot be easily predicted.
6. With a few noteworthy exceptions, there is no cure or established drug treatment for VHFs.

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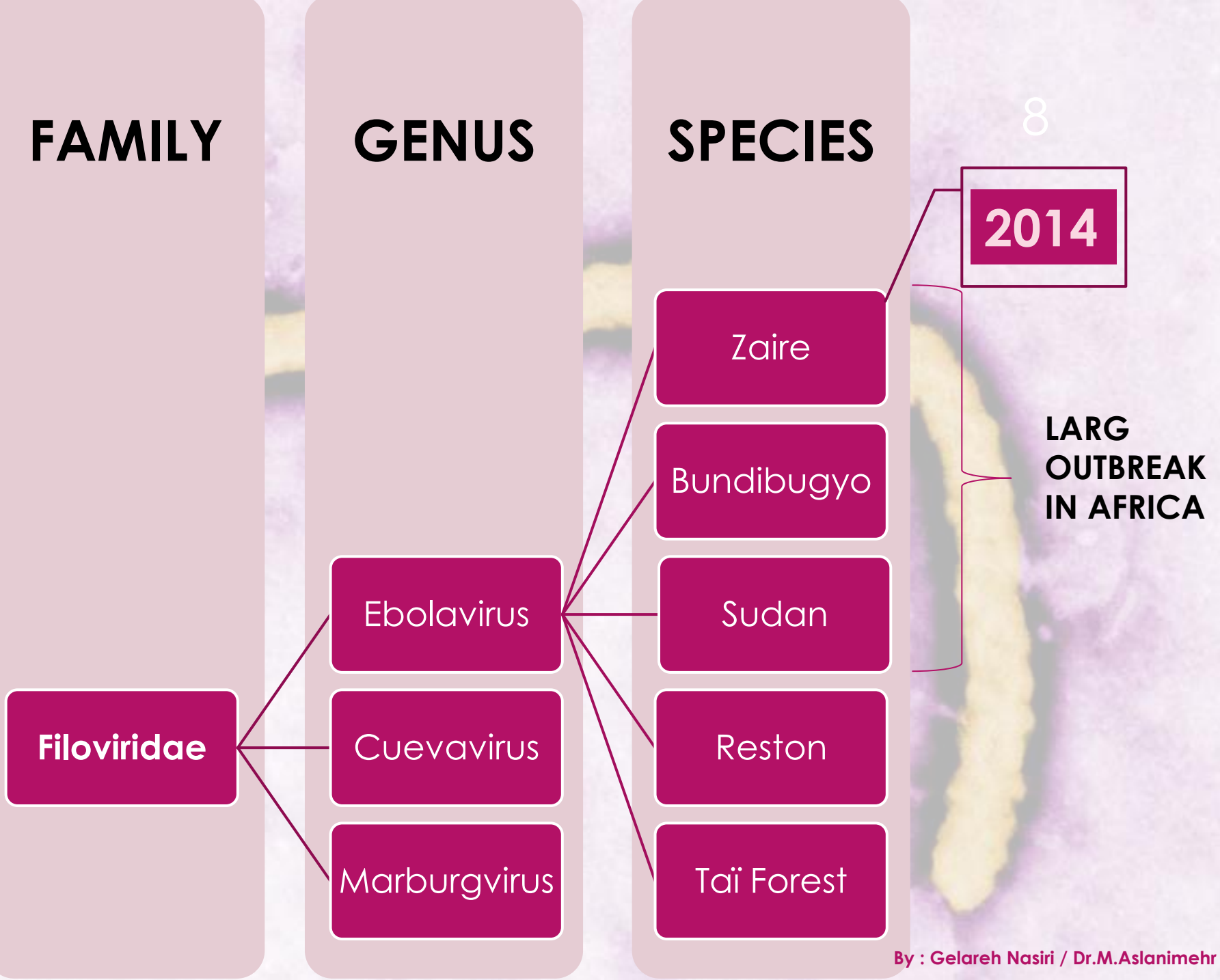
The current outbreak in **west Africa**, (first cases notified in **March 2014**), is **the largest and most complex** Ebola outbreak since the Ebola virus was first discovered in **1976**.

- Order: *Mononegavirales*
  - Family: *Bornaviridae*
  - Family: *Filoviridae*
    - Genus: *Cuevavirus*
    - Genus: *Ebolavirus*
      - Species: *Bundibugyo ebolavirus*
      - Species: *Reston ebolavirus*
      - Species: *Sudan ebolavirus*
      - Species: *Tai Forest ebolavirus*
      - ☆ Species: ***Zaire ebolavirus***
    - Genus: *Marburgvirus*
  - Family: *Nyamiviridae*
  - Family: *Paramyxoviridae*
  - Family: *Rhabdoviridae*

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# Host-Virus Interaction

**Inhibition of host Interferon induction**

Vp35 protein prevents host interferon induction .

**Inhibition of host interferon signalling**

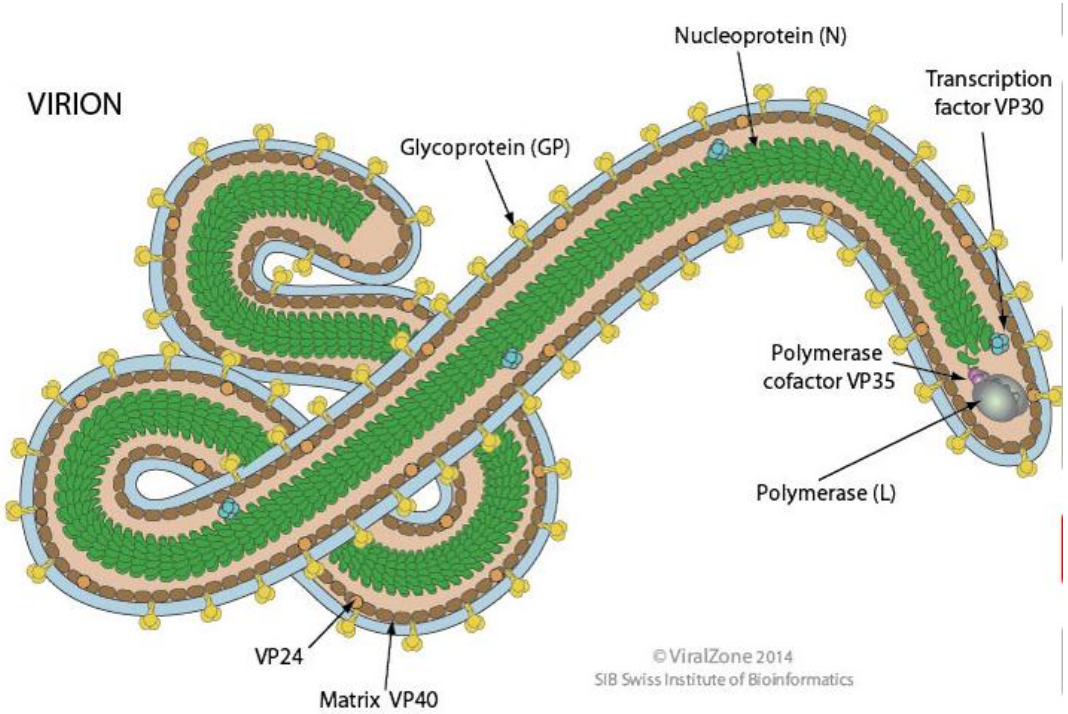
Vp24 protein block interferon signaling

**Antigenic subvertion**

Small Glycoprotein (sGP) is a secreted truncated version of GP that prevent host antibodies anti-GP to effectively neutralize it.

**Inhibition of acquired immune response**

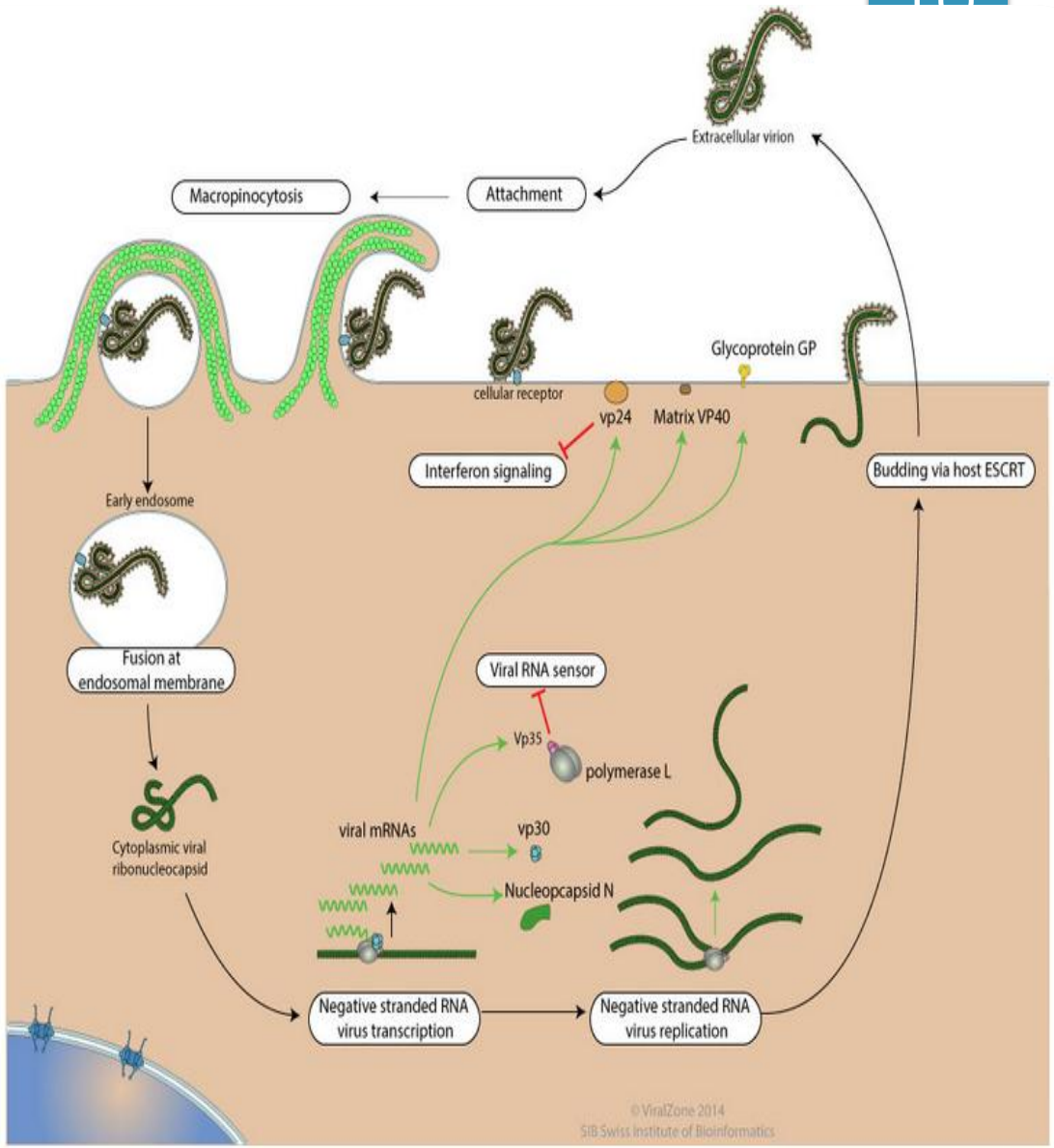
Ebolavirus may encode for a superantigen, thereby inhibiting Vbeta T cells .




Filamentous 970 nm long for Ebolavirus. Diameter is about 80nm.

# Replication Cycle

- Ebola is a **filamentous**, **single-stranded RNA virus** with an unusual, variable-length, branched morphology. The **helical capsid** is enclosed inside a membrane.
- the viral RNA polymerase (L protein) begins to copy the **(-) strand RNA** to make (+) strand transcripts that mimic the structure of mRNA and are translated by host ribosomes.
- The rest of the replicative cycle is unclear, but probably involves assembly of the viral RNA at the host membrane and budding of the helical virus from the cell.

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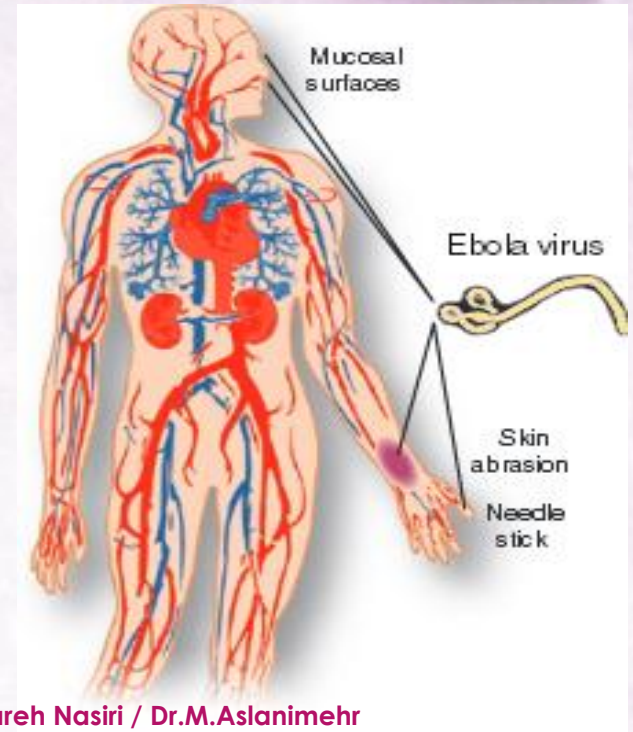
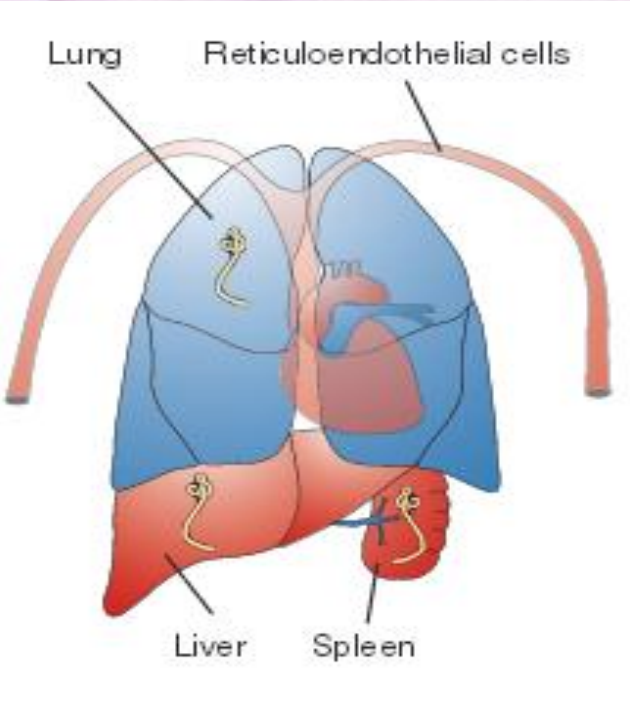
# **EBOLA** PATHOGENESIS

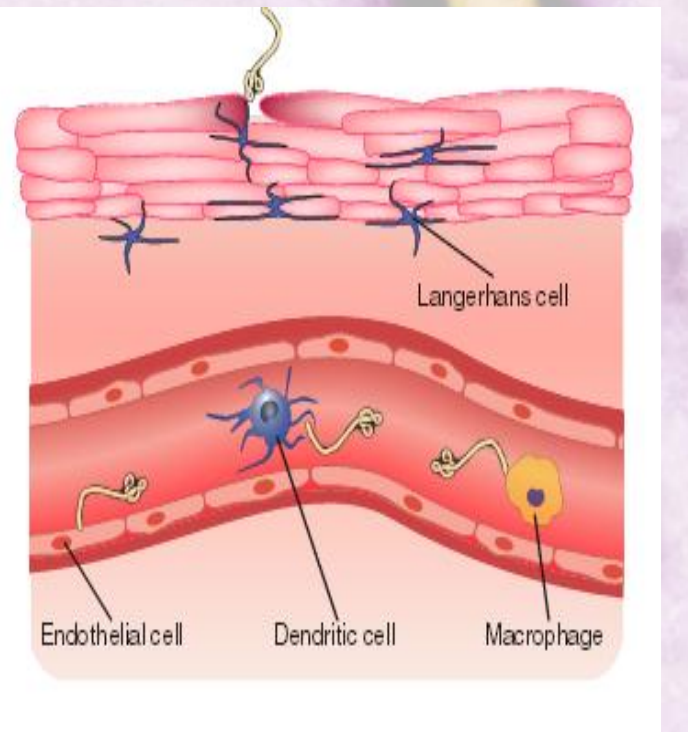
## Primary infection and circulation




## Secondary spread of virus




## Targets of cytotoxicity

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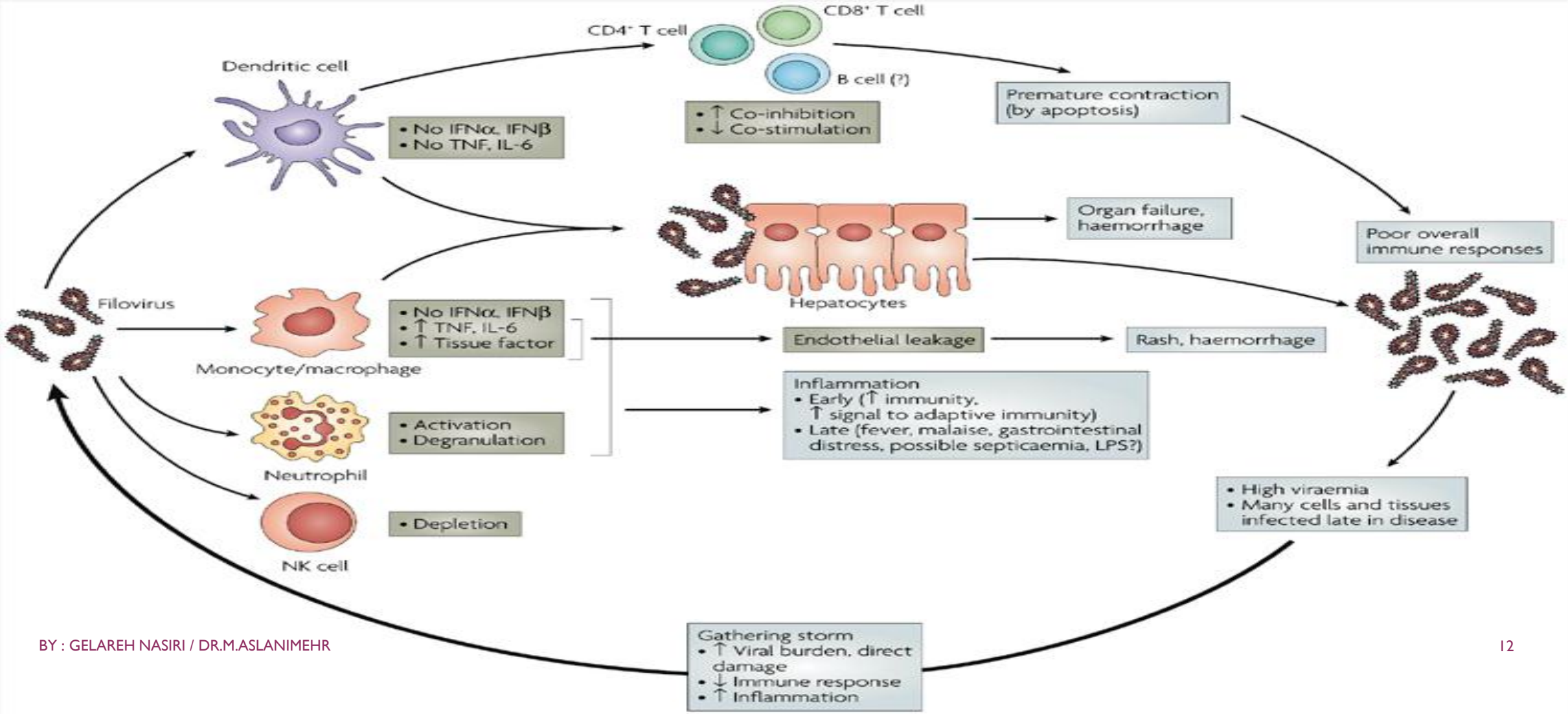
# IMMUNE RESPONSES



## Enzootic Cycle

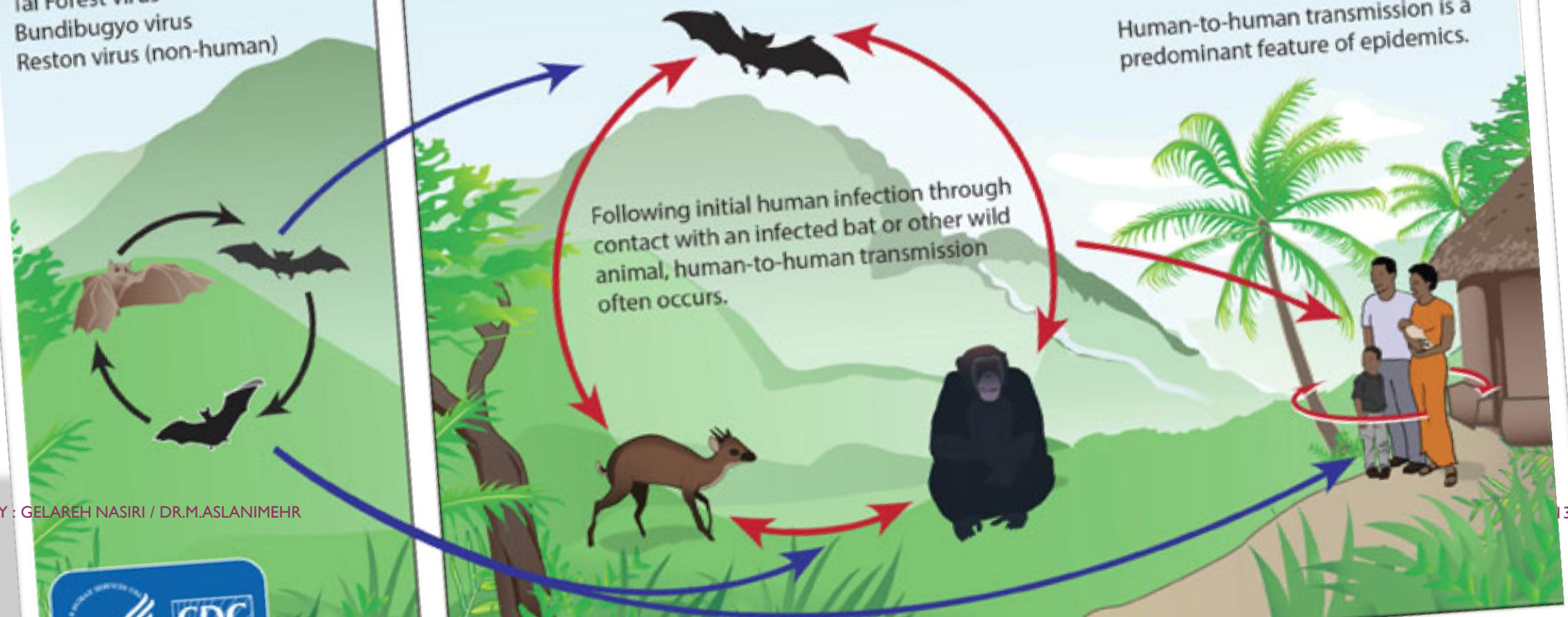
New evidence strongly implicates bats as the reservoir hosts for ebolaviruses, though the means of local enzootic maintainance and transmission of the virus within bat populations remain unknown.

**Ebolaviruses:**

Ebola virus (formerly Zaire virus)
Sudan virus
Taï Forest virus
Bundibugyo virus
Reston virus (non-human)

## Epizootic Cycle

Epizootics caused by ebolaviruses appear sporadically, producing high mortality among non-human primates and duikers and may precede human outbreaks. Epidemics caused by ebolaviruses produce acute disease among humans, with the exception of Reston virus which does not produce detectable disease in humans. Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and an epidemic.



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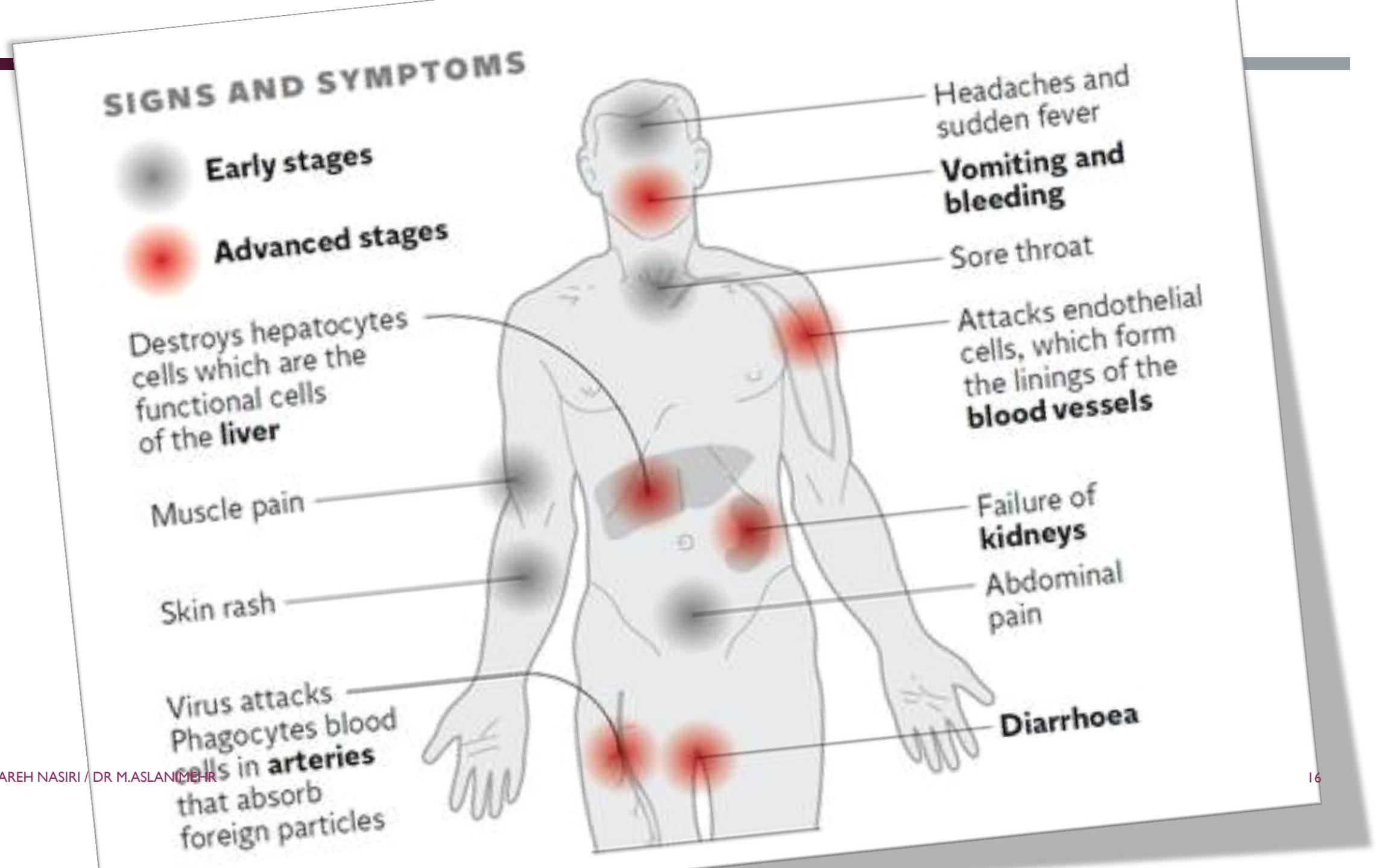
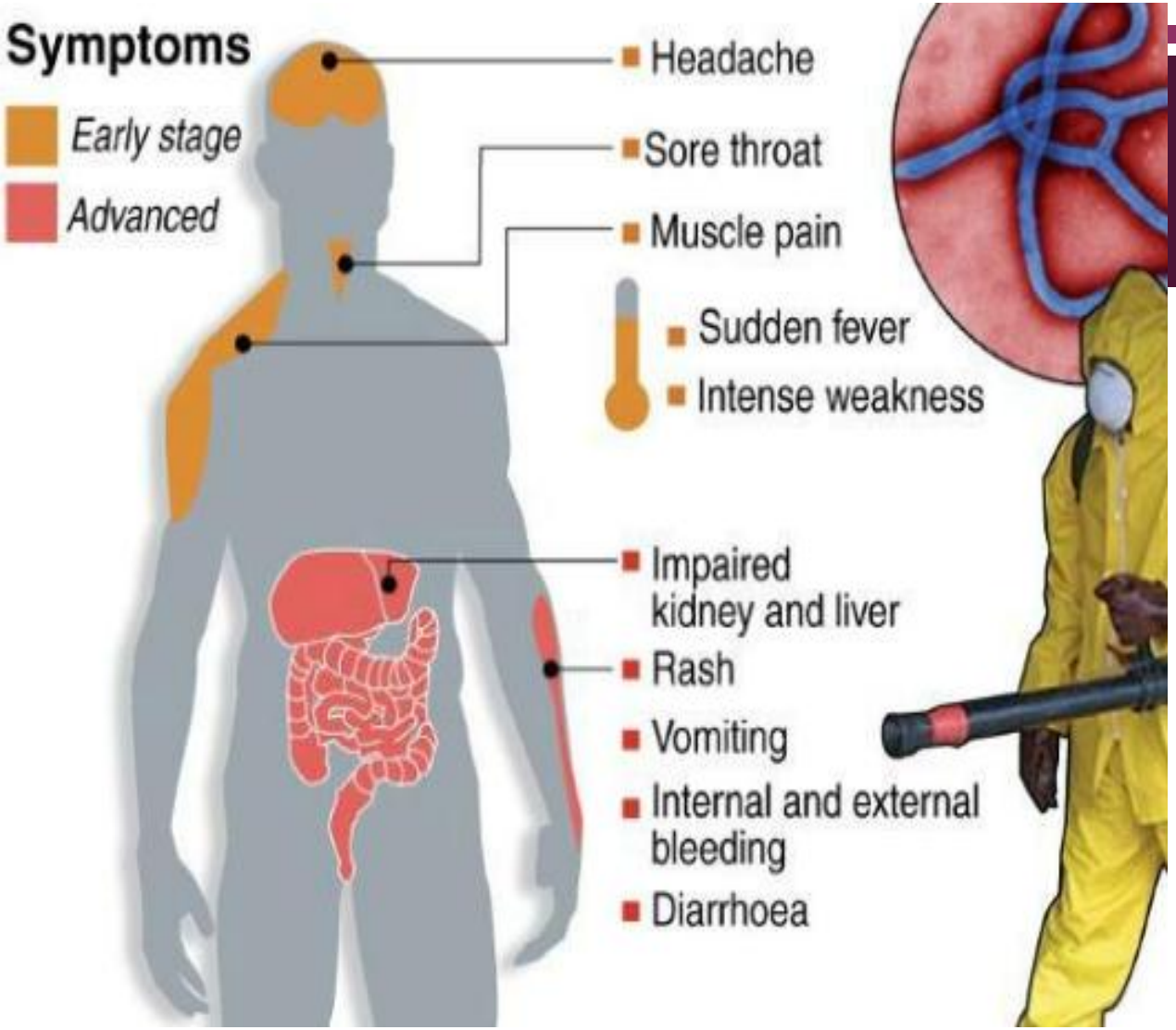
Ebola Virus
Sign & Symptoms


SIGNS AND SYMPTOMS
Early stages
Advanced stages
Destroys hepatocytes cells which are the functional cells of the liver
Muscle pain
Skin rash
Virus attacks Phagocytes blood cells in arteries that absorb foreign particles
Headaches and sudden fever
Vomiting and bleeding
Sore throat
Attacks endothelial cells, which form the linings of the blood vessels
Failure of kidneys
Abdominal pain
Diarrhoea


Symptoms
Early stage
Advanced
Headache
Sore throat
Muscle pain
Sudden fever
Intense weakness
Impaired kidney and liver
Rash
Vomiting
Internal and external bleeding
Diarrhoea

# Ebola virus disease

Ebola, which first appeared in outbreaks in Sudan and DR Congo in 1976, is a severe and often fatal disease with no known specific treatment or vaccine. It has since killed more than 1,500 people in parts of Africa.

## SOURCE

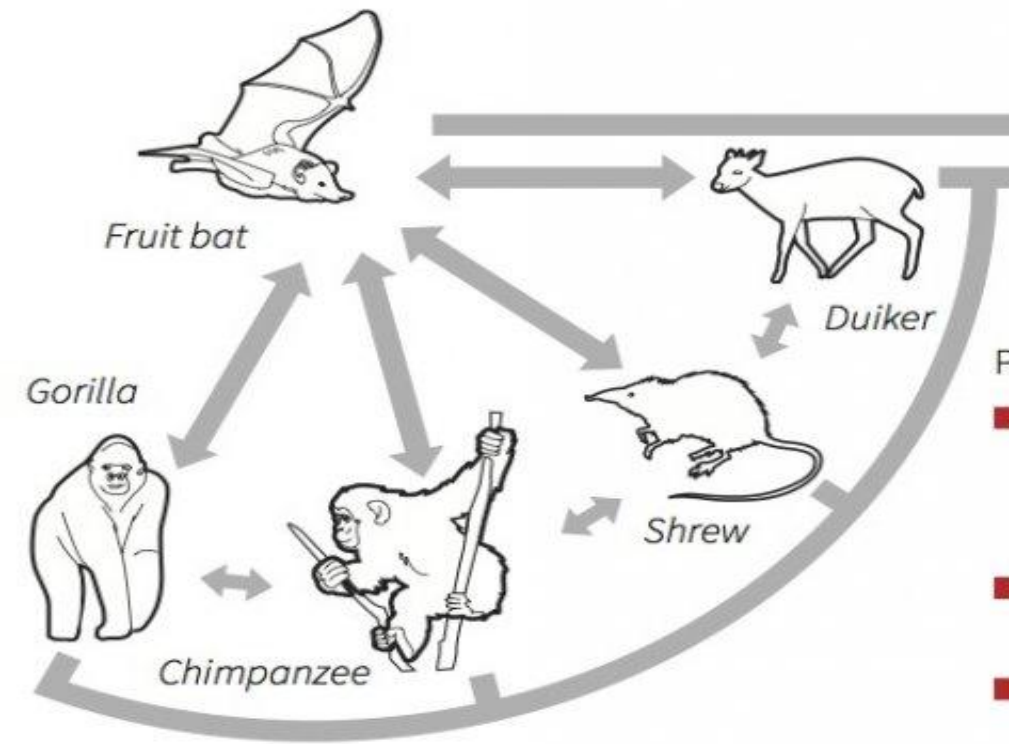
In Africa, particular species of fruit bats are considered possible natural hosts for Ebola virus.

## TRANSMISSION

Infected bats are thought to transmit the disease to humans, or indirectly through other animals which are hunted for their meat.

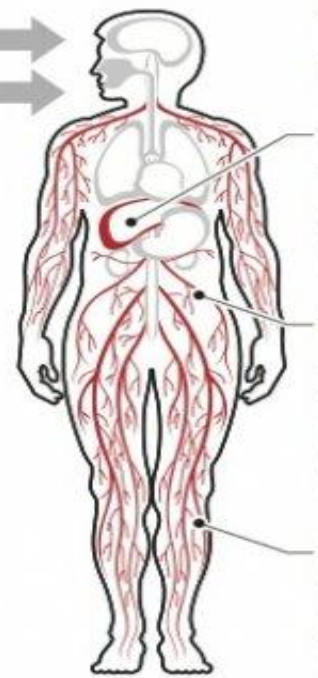
## DAMAGE

Incubation period is from two to 21 days. Death from the disease is often caused by multiple organ failure and tissue death.




Possible routes

- Close contact with the blood, secretions, organs or other bodily fluids of infected or dead animals
- Consumption of infected bushmeat
- Touching objects that have come in contact with the virus.



**Targets in the body**

- Hepatocytes, functional cells of the liver
- Endothelial cells, which form the linings of the blood vessels
- Phagocytes, blood cells that absorb foreign particles

**Symptoms**

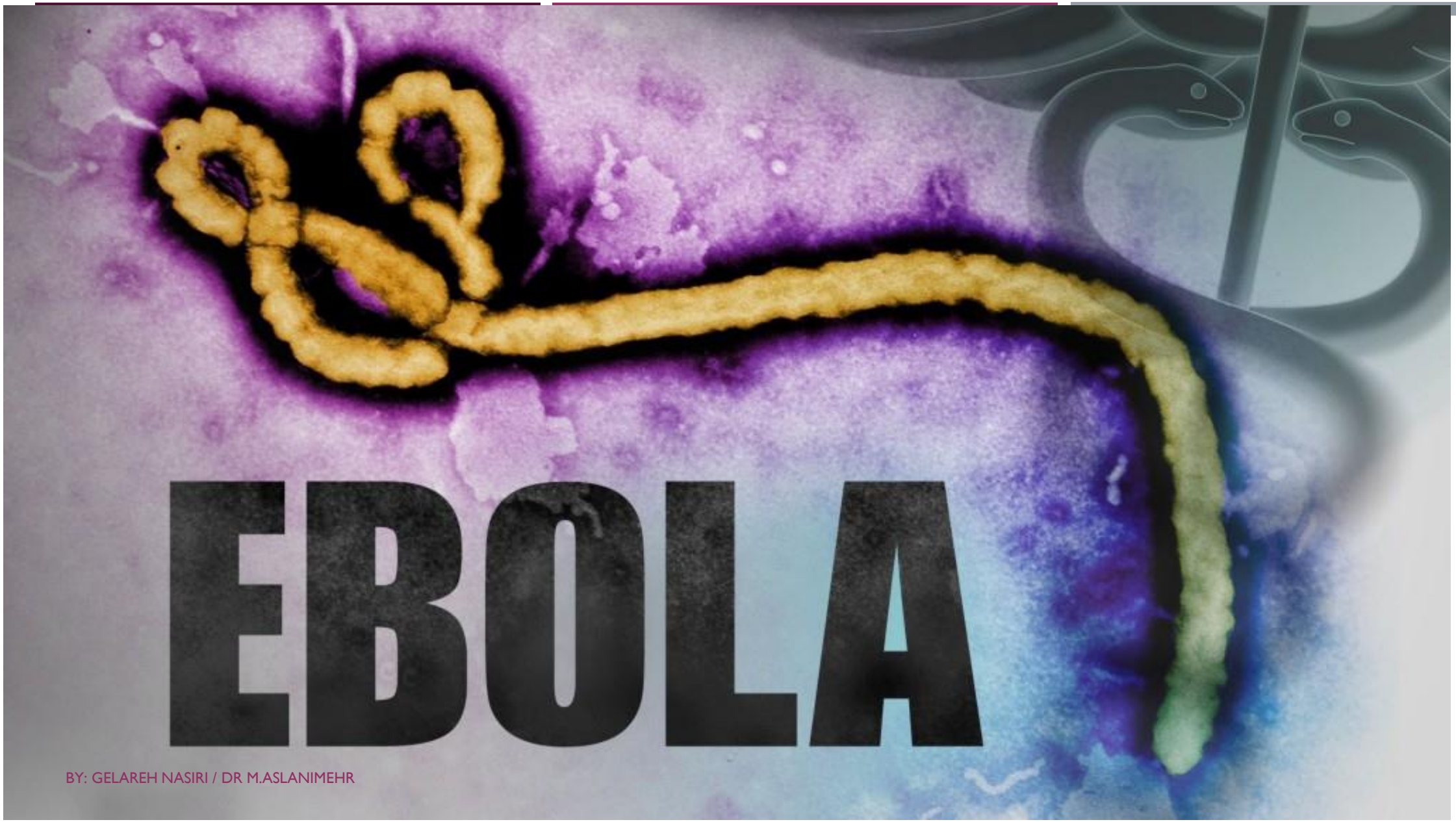
- Fever
- Sore throat
- Severe headache
- Muscle pain
- Intense weakness
- Vomiting
- Diarrhea
- Impaired liver and kidney function
- Internal and external bleeding

Note: List of animals is not exhaustive.

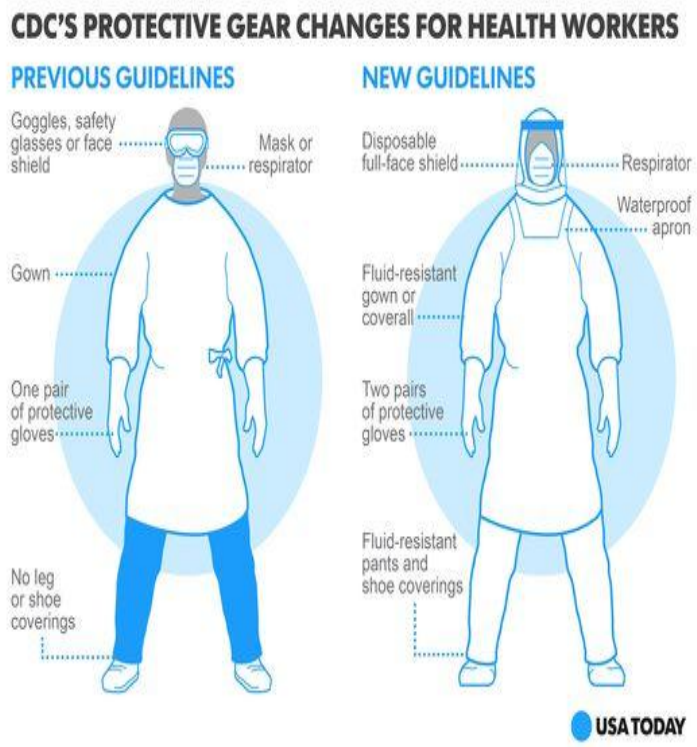
Sources: Centers for Disease Control and Prevention; World Health Organisation

G.Cabrera, 28/03/2014

REUTERS


EBOLA

# Prevention and control




# Prevention and control

Good outbreak control relies on applying a package of interventions, namely case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilisation. Community engagement is key to successfully controlling outbreaks.

Risk reduction messaging should focus on several factors:

From contact with **infected fruit bats** or **monkeys/apes** and **the consumption of their raw meat**. Animals should be handled with **gloves** and **other appropriate protective clothing**. Animal products (blood and meat) should be thoroughly cooked before consumption.

From direct or close contact with people with Ebola symptoms, particularly with their **bodily fluids**. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home. **Regular hand washing** is required after visiting patients in hospital, as well as after taking care of patients at home.

Including **prompt and safe burial of the dead**, identifying people who may have been in contact with someone infected with Ebola, monitoring the health of contacts for **21 days**, the importance of separating the healthy from the sick to prevent further spread, the importance of good hygiene and maintaining a clean environment.

# HC PREVENT IT FROM SPREADING

1 AVOID PHYSIC
SHOWING SIG
CONTINOUS H
AND STOMAC



OUR HANDS REGULARLY WITH SOAP
EAN WATER

2 DO NOT SHAKE HANDS WITH
PERSONS SHOWING SIGNS OF

## Facts about Ebola

You can't get Ebola through air



You can't get Ebola through water

You can't get Ebola through food

You can only get Ebola from touching bodily fluids of a person who is sick with or has died from Ebola, or from exposure to contaminated objects, such as needles. **Ebola poses no significant risk in the United States.**

## Facts about Bushmeat and Ebola

Bushmeat could be infected with germs that can cause sickness in people, including the Ebola virus.

Monkeys and bats are common sources of bushmeat.

AT
WELL

# TRAVEL TO AND FROM EBOLA-AFFECTED COUNTRIES IS LOW-RISK HERE IS WHAT YOU NEED TO KNOW

## WHILE TRAVELLING

If you develop a fever and Ebola symptoms yourself promptly inform airline personnel.

*fever, weakness, muscle pain, headache, and sore throat; followed by vomiting, diarrhoea, bleeding.*

Alert airline personnel about a fellow traveller who has Ebola symptoms:

## AT AIRPORTS AND AT YOUR DESTINATION

Avoid direct physical contact with anyone who is displaying the symptoms of Ebola.

DO NOT touch the body of a person who has died from Ebola.

Use alcohol rub throughout the day. When hands are visibly dirty use soap and water.

Seek prompt medical attention if you have Ebola symptoms.

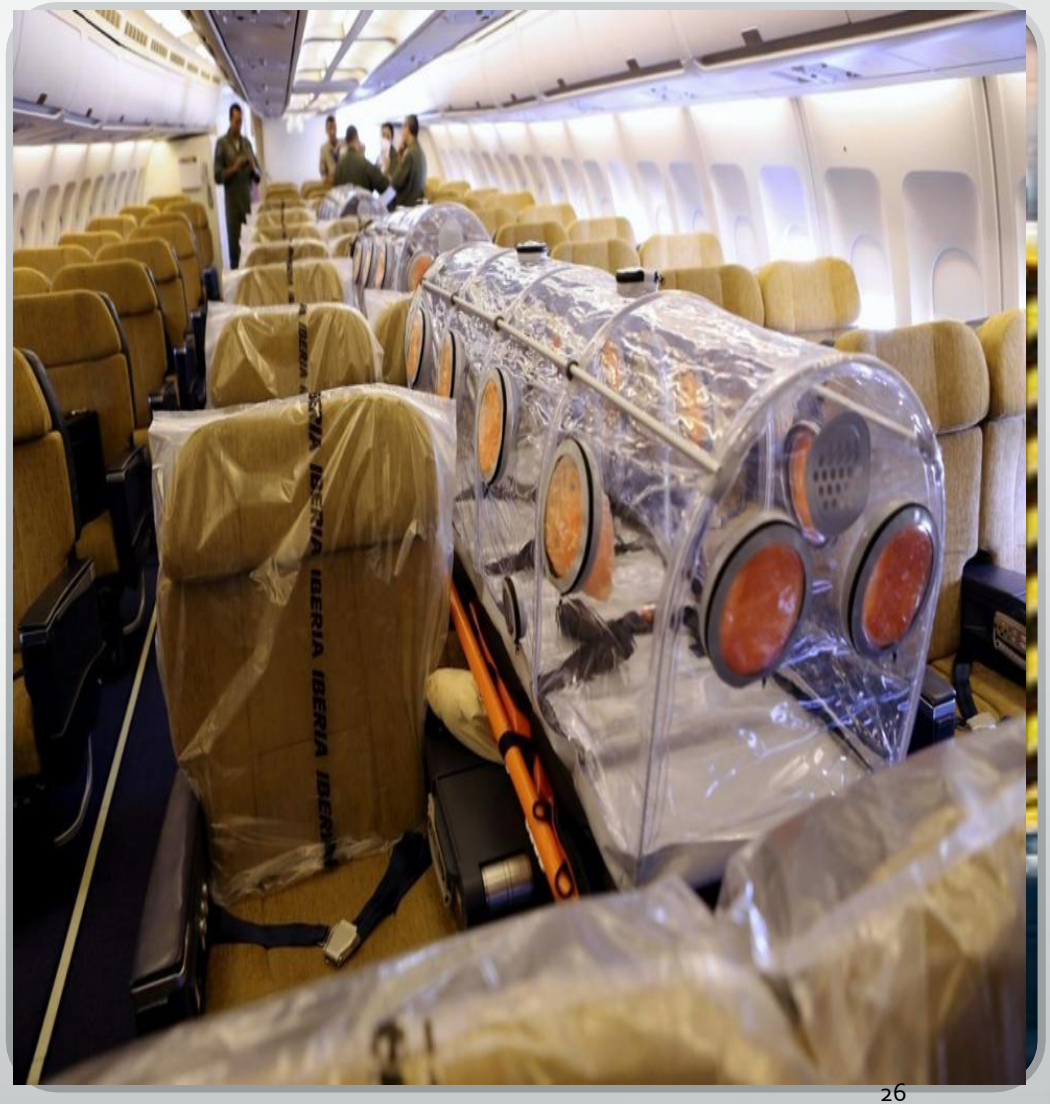
World Health Organization



BY : GELAREH NASIRI / DR.M.ASLANIMEHR

# CONTROLLING INFECTION IN HEALTH-CARE SETTINGS

- ed or confirme
- ent's blood and
-



# Laboratory Findings

- **Low white blood cell** and **platelet counts** and
- **Liver enzyme** tests show **elevated AST** and **ALT**.
- serum levels of **pro-inflammatory cytokines rise.**
- **Urine tests** show **proteinuria**.
- **Blood tests** often indicate **leukopenia**, **thrombocytopenia**, and **hyperproteinemia**.

# Diagnosis

- It can be difficult to distinguish EVD from other infectious diseases such as malaria, typhoid fever and meningitis. Confirmation that symptoms are caused by Ebola virus infection are made using the following investigations:

1. antibody-capture enzyme-linked immunosorbent assay (ELISA)
2. antigen-capture detection tests
3. serum neutralization test
4. reverse transcriptase polymerase chain reaction (RT-PCR) assay
5. electron microscopy
6. virus isolation by cell culture

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# TREATMENT & VACCINES

- Symptoms of Ebola and complications are treated as they appear. The following basic interventions, when used early, can significantly improve the chances of survival:

1. Providing **intravenous fluids** (IV) and **balancing electrolytes** (body salts).
2. Maintaining **oxygen status** and **blood pressure**.
3. Treating **other infections** if they occur.

- There is as yet **no proven treatment available** for EVD. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated.
- **No licensed vaccines are available yet,** but **2 potential vaccines are undergoing human safety testing.**

# TREATMENT & VACCINES

- Supportive care-rehydration with oral or intravenous fluids- and treatment of specific symptoms, improves survival. There is as yet **no proven treatment available** for EVD. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated.
- **No licensed vaccines are available yet**, but **2 potential vaccines are undergoing human safety testing.**

# EBOLA VACCINES


BIDNESS ETC
Ebola
Vaccine

## RECOMBINANT VSV AS A VACCINE VECTOR FOR FILOVIRUSES

VSV is the prototypic member of the family *Rhabdoviridae*, a family of negative-stranded RNA viruses with a simple genome organization encoding 5 structural proteins in the order nucleocapsid (N), phosphoprotein (P), matrix (M), glycoprotein (G), and an RNA-dependent RNA polymerase (L) [21]. VSV causes a disease in cattle, horses, deer, and pigs that is characterized by vesiculation and ulceration of the tongue, oral tissues, feet, and teats [21]. Infected animals typically recover within 2 weeks. Whereas naturally occurring VSV infection of humans is rare, infections have been reported in persons who were directly exposed to infected livestock, who were living within endemic regions, or who were accidentally exposed in laboratories [22–24]. VSV infection of humans usually either is asymptomatic or causes a mild influenza-like illness [22-24]. Among small

*Vesicular Stomatitis Virus–Based*
*nst Ebola and Marburg Virus*

*mann*[3,4,5]

*Microbiology and Immunology, University of Texas Medical Bra*
*Institute of Allergy and Infectious Diseases, National Institut*
*iology Laboratory, Public Health Agency of Canada, and* [5]*Dep*
*University of Manitoba, Winnipeg, Manitoba, Canada*

*The filoviruses, Marburg virus and Ebola virus, cause severe hemorrhagic fever wit*
*humans and nonhuman primates. Among the most-promising filovirus vaccines unde*
*based on recombinant vesicular stomatitis virus (rVSV) that expresses a single filovi*
*place of the VSV glycoprotein (G). Importantly, a single injection of blended rVSV-bas*
*shown to completely protect nonhuman primates against Marburg virus and 3 differe*
*These rVSV-based vaccines have also shown utility when administered as a postexp*
*filovirus infections, and a rVSV-based Ebola virus vaccine was recently used to treat*
*xposure. Here, we review the history of rVSV-based vaccines and pivotal animal studies*
*bating Ebola and Marburg virus infections.*

## RECOMBINANT VSV VECTORS AS PREVENTIVE FILOVIRUS VACCINES

Initial studies using rVSV△G-based filovirus vaccines focused on the ability of these vaccines to protect animals against homologous filovirus challenges. Vaccination of BALB/c mice with a single intraperitoneal injection of as few as 2 PFU of a rVSV△G vector expressing the ZEBOV GP completely protected the animals against a lethal mouse-adapted ZEBOV challenge 28 days after the immunization [41]. Likewise, a single intramuscular vaccination of cynomolgus monkeys with a rVSV△G vector expressing the ZEBOV GP induced strong humoral and cellular immune responses in vaccinated monkeys and elicited complete protection against a high-dose (1000 PFU) intramuscular challenge of homologous ZEBOV given 28 days later [4] (Table 2). However, there was no cross-protection, as subsequent back-challenge of the ZEBOV-surviving macaques

# Antibodies are necessary for rVSV/ZEBOV-GP–mediated protection against lethal Ebola virus challenge in nonhuman primates

Andrea Marzi[a,1], Flora Engelmann[b,1], Friederike Feldmann[c], Kristen Haberthur[d], W. Lesley Shupert[e], Douglas Brining[e], Dana P. Scott[e], Thomas W. Geisbert[f,g], Yoshihiro Kawaoka[h,i,j], Michael G. Katze[k,l], Heinz Feldmann[a,2], and Ilhem Messaoudi[b,d,m,2]

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Edited by Tilahun D. Yilma, University of California, Davis, CA, and approved December 12, 2012 (received for review June 5, 2012)

**Ebola viruses cause hemorrhagic disease in humans and nonhuman primates with high fatality rates. These viruses pose a significant health concern worldwide due to the lack of approved therapeutics and vaccines as well as their potential misuse as bioterrorism agents. Although not licensed for human use, recombinant vesicular stomatitis virus (rVSV) expressing the filovirus glycoprotein (GP) has been shown to protect macaques from Ebola virus and Marburg virus infections, both prophylactically and postexposure in a homologous challenge setting. However, the immune mechanisms of protection conferred by this vaccine platform remain poorly understood. In this study, we set out to investigate the role of humoral versus cellular immunity in rVSV vaccine-mediated protection against lethal *Zaire ebolavirus* (ZEBOV) challenge. Groups of cynomolgus macaques were depleted of CD4+ T, CD8+ T, or CD20+ B cells before and during vaccination with rVSV/ZEBOV-GP. Unfortunately, CD20-depleted animals generated a robust IgG response. Therefore, an additional group of vaccinated animals were depleted of CD4+ T cells during challenge. All animals were subsequently challenged with a lethal dose of ZEBOV. Animals depleted of CD8+ T cells survived, suggesting a minimal role for CD8+ T cells in vaccine-mediated protection. Depletion of CD4+ T cells during vaccination caused a complete loss of glycoprotein-specific antibodies and abrogated vaccine protection. In contrast, depletion of CD4+ T cells during challenge resulted in survival of the animals, indicating a minimal role for CD4+ T-cell immunity in rVSV-mediated protection. Our results suggest that antibodies play a critical role in rVSV-mediated protection against ZEBOV.**

Ebola viruses (EBOVs) are enveloped, negative single-stranded RNA viruses with a genome of ~19 kb in size that belong to the *Filoviridae* family. There are five species of EBOV: *Zaire ebolavirus* (ZEBOV), *Sudan ebolavirus* (SEBOV), *Bundibugyo ebolavirus* (BEBOV), *Côte d'Ivoire ebolavirus* (CIEBOV), and *Reston ebolavirus* (REBOV). The species vary in their pathogenicity, with ZEBOV being most pathogenic (up to 90% case fatality), followed by SEBOV and BEBOV, with up to 50%. CIEBOV and REBOV have been shown to be lethal in nonhuman primates (NHPs), but only CIEBOV has been associated with one severe human case so far (1, 2). Currently, Old World macaques, notably cynomolgus and rhesus macaques, are the gold standard animal model for studying ZEBOV pathogenesis and testing vaccines and therapeutics. Both macaque species are highly susceptible to ZEBOV, with development of viral hemorrhagic fever and 100% lethality (3).

Although there is no licensed vaccine or treatment available for EBOV infections, a number of vaccine platforms have proven to be efficacious in nonhuman primate challenge studies. These platforms include DNA, recombinant adenovirus (rAd) (alone or in combination with DNA prime), virus-like particles (VLPs), human parainfluenza virus 3, and recombinant vesicular stomatitis virus (rVSV) (4). Most of these vaccines express the ZEBOV glycoprotein (GP) as the immunogen. The rVSV approach has proven to be among the most promising vaccine platforms for ZEBOV. The rVSV vectors are based on a reverse genetics system for VSV serotype Indiana (5) and have also been used to develop immunization strategies against other viruses, like influenza virus (6) and simian/HIV (SHIV) (7). One dose of this vaccine can successfully protect rodents and nonhuman primates from lethal ZEBOV infection (8, 9). Additionally, a single dose of this vaccine confers partial protection postexposure in immunocompetent rodents and nonhuman primates as well as preexposure in immunocompromised SHIV-infected rhesus macaques against lethal ZEBOV challenge (10–12).

Little is known about the mechanisms of protection of the rVSV vectors against ZEBOV infection, although it appears that both cellular and humoral immune responses are required in the nonhuman primate infection model. In this study, we investigated the role of CD4+ T-cell, CD8+ T-cell, or CD20+ B-cell responses in conferring protection following vaccination with rVSV/ZEBOV-GP. To that end, we depleted these cell populations using monoclonal antibodies before and during the vaccination period with rVSV/ZEBOV-GP. Following depletions, we characterized the cellular and humoral response against ZEBOV-GP in vaccinated animals. Cellular responses were very low in all of the groups including the nondepleted animals. Interestingly, with the exception of the CD4+ T-cell–depleted group, all of the animals developed a ZEBOV-GP–specific IgG response. This included the CD20+ B-cell–depleted animals, suggesting that we were unable to completely eliminate the B cells in this group. More importantly, only the CD4-depleted animals succumbed to ZEBOV infection. To confirm that antibodies and not effector CD4+ T cells are critical for protection, additional animals were vaccinated and depleted of

MICROBIOLOGY

Author contributions: A.M., Y.K., M.G.K., H.F., and I.M. designed research; A.M., F.E., F.F., K.H., W.L.S., D.B., D.P.S., and H.F. performed research; A.M., H.F., and I.M. analyzed data; and A.M., T.W.G., H.F., and I.M. wrote the paper.

The authors declare no conflict of interest.

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# WHO welcomes Swissmedic approval of Ebola vaccine trial at Lausanne University Hospital

Statement
28 October 2014

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The World Health Organization (WHO) welcomes the approval by Swissmedic, the Swiss regulatory authority for therapeutic products, for a trial with an experimental Ebola vaccine at the Lausanne University Hospital (CHUV). This marks the latest step towards bringing safe and effective Ebola vaccines for testing and implementation as quickly as possible.

Approval means that the vaccine can be used on approximately 120 individuals in Lausanne. The trial, which is receiving support from WHO, is the latest in a series of trials that are ongoing in Mali, the United Kingdom, and the United States.

## About the vaccine

The vaccine is based on a genetically modified chimpanzee adenovirus ("ChAd-Ebola"; Chimpanzee-Adenovirus chAD3-ZEBOV). The trial will test the safety of the vaccine and its capacity to induce an immune response. Results from the CHUV trial will – together with the results of other centres involved – provide the basis for planning subsequent trials involving several thousand participants, and for choosing vaccine dose-level for efficacy trials.

Developed by the US National Institute of Allergy and Infectious Diseases (NIAID) and pharmaceutical company GlaxoSmithKline, the vaccine consists of a virus that is rendered harmless and used as genetic carrier for one Ebola protein. The application, submitted at the end of September 2014, was handled as a priority, given the dimensions of the Ebola epidemic in West Africa.

## Vaccine trials

The trial is one of two in Switzerland coordinated by WHO. A second vaccine, rVSV-ZEBOV, is to be tested at the Geneva University Hospitals, concurrent to the Lausanne trial.

"These are dosing and safety trials being held in advance of Phase II and III trials currently scheduled for late 2014-early 2015," says Marie-Paule Kieny, Assistant Director-General for Health Systems and Innovation at WHO. "If shown to be safe and effective, either of the vaccines could be scaled up for production during the first quarter of next year, with millions of doses produced for wide distribution in high-risk countries."

Trials in Lausanne will begin this week, with first results expected in December 2014.


## About the vaccine

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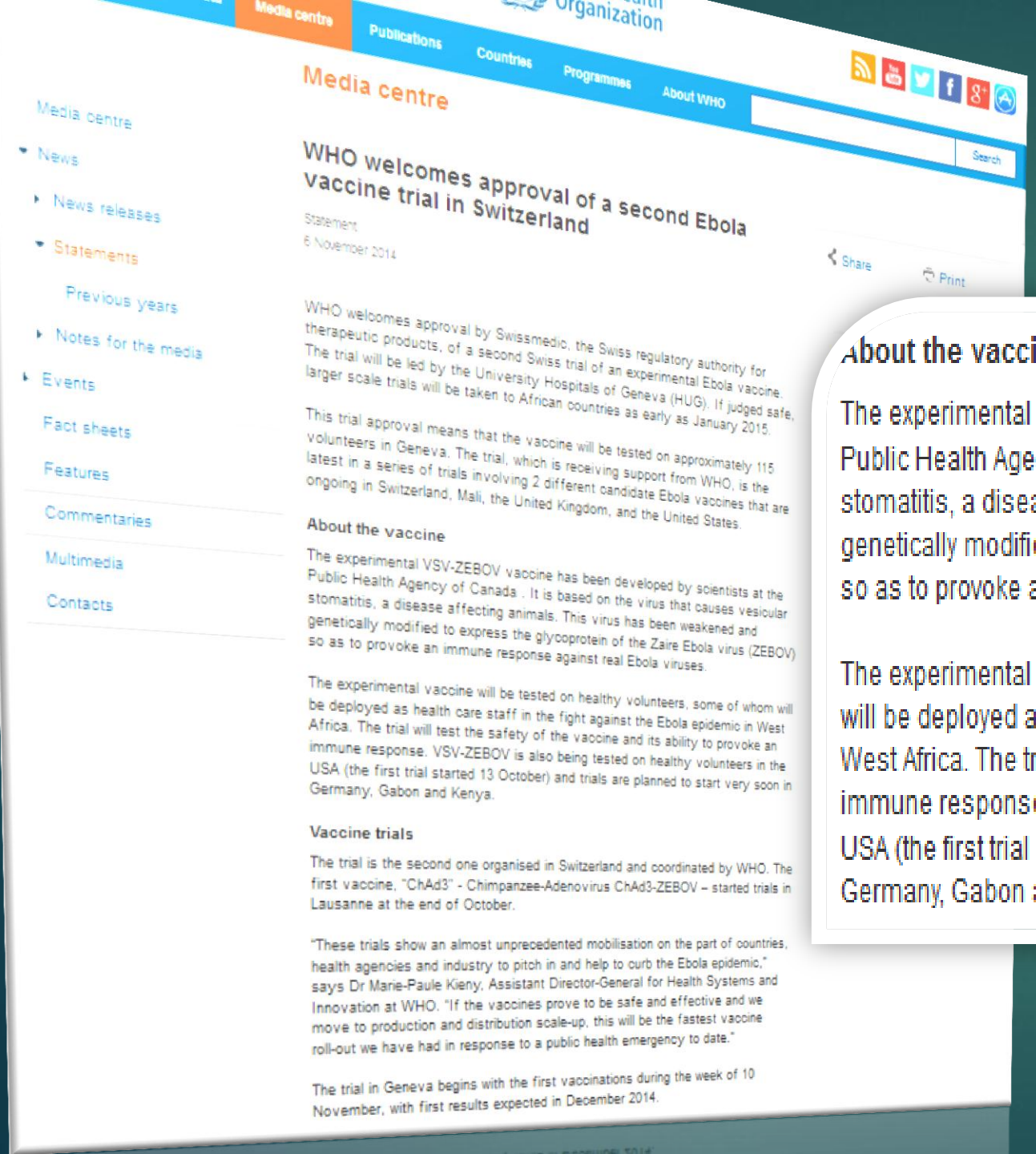
By : Gelareh Nasiri / Dr.M.Aslanimehr



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## WHO welcomes approval of a second Ebola vaccine trial in Switzerland

Statement
6 November 2014

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WHO welcomes approval by Swissmedic, the Swiss regulatory authority for therapeutic products, of a second Swiss trial of an experimental Ebola vaccine. The trial will be led by the University Hospitals of Geneva (HUG). If judged safe, larger scale trials will be taken to African countries as early as January 2015.

This trial approval means that the vaccine will be tested on approximately 115 volunteers in Geneva. The trial, which is receiving support from WHO, is the latest in a series of trials involving 2 different candidate Ebola vaccines that are ongoing in Switzerland, Mali, the United Kingdom, and the United States.

### About the vaccine

The experimental VSV-ZEBOV vaccine has been developed by scientists at the Public Health Agency of Canada . It is based on the virus that causes vesicular stomatitis, a disease affecting animals. This virus has been weakened and genetically modified to express the glycoprotein of the Zaire Ebola virus (ZEBOV) so as to provoke an immune response against real Ebola viruses.

The experimental vaccine will be tested on healthy volunteers, some of whom will be deployed as health care staff in the fight against the Ebola epidemic in West Africa. The trial will test the safety of the vaccine and its ability to provoke an immune response. VSV-ZEBOV is also being tested on healthy volunteers in the USA (the first trial started 13 October) and trials are planned to start very soon in Germany, Gabon and Kenya.

### Vaccine trials

The trial is the second one organised in Switzerland and coordinated by WHO. The first vaccine, "ChAd3" - Chimpanzee-Adenovirus ChAd3-ZEBOV – started trials in Lausanne at the end of October.

"These trials show an almost unprecedented mobilisation on the part of countries, health agencies and industry to pitch in and help to curb the Ebola epidemic," says Dr Marie-Paule Kieny, Assistant Director-General for Health Systems and Innovation at WHO. "If the vaccines prove to be safe and effective and we move to production and distribution scale-up, this will be the fastest vaccine roll-out we have had in response to a public health emergency to date."

The trial in Geneva begins with the first vaccinations during the week of 10 November, with first results expected in December 2014.


## About the vaccine

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# The structure of the C-terminal domain of the *Zaire ebolavirus* nucleoprotein

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*Ebolavirus* (EBOV) causes severe hemorrhagic fever with a mortality rate of up to 90%. EBOV is a member of the order *Mononegavirales* and, like other viruses in this taxonomic group, contains a negative-sense single-stranded (ss) RNA. The EBOV ssRNA encodes seven distinct proteins. One of them, the nucleoprotein (NP), is the most abundant viral protein in the infected cell and within the viral nucleocapsid. Like other EBOV proteins, NP is multifunctional. It is tightly associated with the viral genome and is essential for viral transcription, RNA replication, genome packaging and nucleocapsid assembly prior to membrane encapsulation. NP is unusual among the *Mononegavirales* in that it contains two distinct regions, or putative domains, the C-terminal of which shows no homology to any known proteins and is purported to be a hub for protein–protein interactions within the nucleocapsid. The atomic structure of NP remains unknown. Here, the boundaries of the N- and C-terminal domains of NP from Zaire EBOV are defined, it is shown that they can be expressed as highly stable recombinant proteins in *Escherichia coli*, and the atomic structure of the C-terminal domain (residues 641–739) derived from analysis of two distinct crystal forms at 1.98 and 1.75 Å resolution is described. The structure reveals a novel tertiary fold that is distantly reminiscent of the β-grasp architecture.

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Dank U
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Grazie
Thank you
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Takk
Gracias
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